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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of :

Andreas MENRAD et al.

Serial No.: 09/942,117

Filed: August 30, 2001



Group Art Unit

Examiner: Unassigned

For: RECEPTOR OF THE ED_b-FIBRONECTIN DOMAINS

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to initial examination, please amend the above-identified application as follows:

IN THE CLAIMS:

Please amend the claims as follows:

3. (Amended) A protein, according to claim 1,
- a) that has the ability to bind specifically to the ED_b-fibronectin domains and that comprises the $\alpha 2\beta 1$ chain of the integrin;
 - b) that is expressed or activated specifically in endothelial cells;
 - c) that is expressed or activated specifically in stromal cells of a tumor;
 - d) that is expressed or activated specifically in tumor cells;
 - e) whose binding to the ED_b-fibronectin domains is inhibited by a polypeptide and that comprises the α chain of the integrin; and
 - f) that has an apparent molecular weight of 120-130 kDa for the light chain and 150-160 kDa for the heavy chain, determined by SDS-polyacrylamide gel electrophoresis.

4. (Amended) Protein according to claim 1, characterized in that the endothelial cells are proliferating endothelial cells.

17. (Amended) Antibody that is able to bind to a protein according to claim 1.

19. (Amended) Antibody according to claim 17 that is able to inhibit effects that are specific to the ED_b-fibronectin domains.

20. (Amended) Antibody according to claims 17, whereby the binding and inhibition are carried out in vitro and/or in vivo.

21. (Amended) Antibody according to claims 17, wherein it is monoclonal or recombinant.

22. (Amended) Antibody, according to claim 17, wherein it is an scFv fragment.

23. (Amended) Cell that expresses a protein according to claims 1.

24. (Amended) Cell that expresses an antibody according to claim 17.

25. (Amended) Phage that expresses an antibody according to claim 17.

26. (Amended) Process for screening compounds that bind to a receptor of the ED_b-fibronectin domains, whereby the process comprises:

Comparison of a response of cells in the presence of one or more of these compounds with the control response of said cells in the absence of these compounds, whereby the cells express a protein according to claim 1 or

comprise a nucleic acid that codes for this protein, and whereby the response or the control response is mediated by a receptor of the ED_b-fibronectin domains.

28. (Amended) Process according to claim 26, wherein a binding region of the ED_b-fibronectin domains comprises sequences SEQ ID NOS: 1-4 or portions thereof.

31. (Amended) Process according to claim 26, whereby the compounds are selected from the group that comprises antibodies, artificial antibodies, antibody fragments, peptides, low-molecular compounds, aptamers and Spiegelmers.

34. (Amended) Process for screening compounds that bind to the ED_b-fibronectin domains, whereby the process comprises:

a) Bringing cells into contact with a fixed concentration of a protein that comprises the ED_b-fibronectin domains or a protein with one of the sequences that are represented in SEQ ID NOS: 1-4, in the presence of different concentrations of one or more of the compounds; and

b) Determination of differences in the response of cells to the protein that comprises the ED_b-fibronectin domains or a protein with one of the sequences that are represented in SEQ ID NOS: 1-4, in the presence of the compounds in comparison to the control response of cells to the protein that comprises the ED_b-fibronectin domains or a protein with one of the sequences that are represented in SEQ ID NOS: 1-4, in the absence of these compounds, whereby

the cells express a protein according to claim 1 or

comprise a nucleic acid that codes for this protein,

and whereby the response or the control response is mediated by a receptor of the ED_b-fibronectin domains.

38. (Amended) Process according to claim 34, whereby the compounds are selected from the group that comprises antibodies, artificial antibodies, antibody fragments, peptides, low-molecular substances, aptamers and Spiegelmers.

40. (Amended) Use of a protein according to claim 1 for screening compounds that bind to a receptor of the ED_b-fibronectin domains or the ED_b-fibronectin domains.

41. (Amended) Use of a cell according to claim 23 for screening compounds that bind to a receptor of the ED_b-fibronectin domains or the ED_b-fibronectin domains.

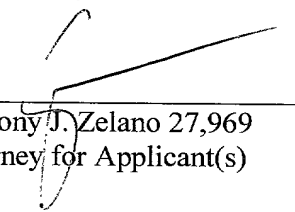
43. (Amended) Use of a protein according to claim 1 to develop antibodies or scFv-fusion proteins for diagnostic or therapeutic purposes.

44. (Amended) Use of a cell according to claim 23 to develop antibodies or scFv-fusion proteins for diagnostic or therapeutic purposes.

REMARKS

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



Anthony J. Zelano 27,969
Attorney for Applicant(s)

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please amend the claims as follows:

3. (Amended) A protein, according to claim 1 [claims 1 to 2],
- a) that has the ability to bind specifically to the ED_b-fibronectin domains and that comprises the $\alpha 2\beta 1$ chain of the integrin;
 - b) that is expressed or activated specifically in endothelial cells;
 - c) that is expressed or activated specifically in stromal cells of a tumor;
 - d) that is expressed or activated specifically in tumor cells;
 - e) whose binding to the ED_b-fibronectin domains is inhibited by a polypeptide and that comprises the α chain of the integrin; and
 - f) that has an apparent molecular weight of 120-130 kDa for the light chain and 150-160 kDa for the heavy chain, determined by SDS-polyacrylamide gel electrophoresis.
4. (Amended) Protein according to claim 1 [claims 1 to 3], characterized in that the endothelial cells are proliferating endothelial cells.
17. (Amended) Antibody that is able to bind to a protein according to claim 1 [one of claims 1-10].
19. (Amended) Antibody according to claim 17 [one of claims 17-18] that is able to inhibit effects that are specific to the ED_b-fibronectin domains.
20. (Amended) Antibody according to claim 17 [one of claims 17-18], whereby the binding and inhibition are carried out in vitro and/or in vivo.
21. (Amended) Antibody according to claim 17 [one of claims 17-20], wherein it is monoclonal or recombinant.
22. (Amended) Antibody, according to claim 17 [one of claims 17-21], wherein it is an scFv fragment.

23. (Amended) Cell that expresses a protein according to claim 1 [one of claims 1-10].
24. (Amended) Cell that expresses an antibody according to claim 17 [one of claims 17-22].
25. (Amended) Phage that expresses an antibody according to claim 17 [one of claims 17-22].
26. (Amended) Process for screening compounds that bind to a receptor of the ED_b-fibronectin domains, whereby the process comprises:
comparison of a response of cells in the presence of one or more of these compounds with the control response of said cells in the absence of these compounds, whereby the cells express a protein according to claim 1 [one of claims 1-10] or
comprise a nucleic acid that codes for this protein, and whereby the response or the control response is mediated by a receptor of the ED_b-fibronectin domains.
28. (Amended) Process according to claim 26 [one of claims 26-27], wherein a binding region of the ED_b-fibronectin domains comprises sequences SEQ ID NOS: 1-4 or portions thereof.
31. (Amended) Process according to claim 26 [one of claims 26-30], whereby the compounds are selected from the group that comprises antibodies, artificial antibodies, antibody fragments, peptides, low-molecular compounds, aptamers and Spiegelmers.
34. (Amended) Process for screening compounds that bind to the ED_b-fibronectin domains, whereby the process comprises:
 - a) Bringing cells into contact with a fixed concentration of a protein that comprises the ED_b-fibronectin domains or a protein with one of the sequences that are represented in SEQ ID NOS: 1-4, in the presence of different concentrations of one or more of the compounds; and
 - b) Determination of differences in the response of cells to the protein that comprises the ED_b-fibronectin domains or a protein with one of the sequences that are represented in SEQ ID NOS: 1-4, in the presence of the compounds in comparison to the control response of cells to the protein

that comprises the ED_b-fibronectin domains or a protein with one of the sequences that are represented in SEQ ID NOS: 1-4, in the absence of these compounds, whereby

the cells express a protein according to claim 1 [one of claims 1-10] or

comprise a nucleic acid that codes for this protein,

and whereby the response or the control response is mediated by a receptor of the ED_b-fibronectin domains.

38. (Amended) Process according to claim 34 [one of claims 34-37], whereby the compounds are selected from the group that comprises antibodies, artificial antibodies, antibody fragments, peptides, low-molecular substances, aptamers and Spiegelmers.

40. (Amended) Use of a protein according to claim 1 [one of claims 1-10 or an antibody according to one of claims 17-22] for screening compounds that bind to a receptor of the ED_b-fibronectin domains or the ED_b-fibronectin domains.

41. (Amended) Use of a cell according to claim 23 [one of claims 23-24] for screening compounds that bind to a receptor of the ED_b-fibronectin domains or the ED_b-fibronectin domains.

43. (Amended) Use of a protein according to claim 1 [one of claims 1-10] to develop antibodies or scFv-fusion proteins for diagnostic or therapeutic purposes.

44. (Amended) Use of a cell according to claim 23 [one of claims 23-24] to develop antibodies or scFv-fusion proteins for diagnostic or therapeutic purposes.